Remarks

Claims 15-16, 26, and 60 have been canceled without prejudice or disclaimer; Applicants preserve the right to pursue the cancelled subject matter in one or more continuation or divisional applications. Claims 5-6, 24, 27, 32, 58, 61, 66, 84 and 102 have been amended as noted herein in accordance with 37 C.F.R. § 1.116 to comply with requirements set forth in the prior office actions and/or to present the claims in better form for consideration on appeal in the event that the prior rejections have not been overcome or obviated. Support for the amended claims is found throughout the specification as filed, including at paragraphs 203, 233, 271, 395, 263 and also in original claims 26-27. Thus, no new matter has been added.

Claims 1, 5-14, 17-25, 27-37, 41-46, 51-52, 55-59, 61-67, 69-70, 79-86 and 97-104 are pending; claims 22-32, 57-66, 79-86 and 97-104 have been withdrawn pending rejoinder. Applicants note that it is unclear from the Office Action whether or not the Examiner intended to withdraw claim 56; the claim status is indicated as "Original" pending clarification in the next action. Claims 1, 7-14, 17-21, 33-37, 41-46, 51-52, 55, 67, and 69-70 have been allowed; in light of the present amendments and arguments, Applicants believe that all claims are now in condition for allowance.

I. Amendments to the Specification/Trademark Usage

The Examiner has maintained the objection to the specification, alleging that generic terminology has not been appropriately included for trademarks. In response, Applicants have amended the specification to add generic terminology as appropriate. Applicants have also corrected the capitalization and trademark indicia that appear to have been erroneously included for certain generic terms. In light of the amendments, Applicants believe that the trademark usage in the instant application is correct, and thus the instant objection should be reconsidered and withdrawn.

II. Rejection of Claims 5-6 and 15-16

The Examiner has rejected claims 5, 6, 15, and 16 as allegedly lacking enablement. Specifically, the Examiner contends that the specification does not provide enablement for

antibodies that inhibit heptamerization of PA63 and PA63 binding to EF or LF, inhibition of PA-mediated translocation of EF or LF across a membrane or antibodies with K_D less than or equal to 10^{-11} M or 10^{-12} M.

In response, while Applicants disagree and maintain that claims 15-16 were fully enabled, these claims have been canceled without prejudice or disclaimer, thereby obviating any rejection thereof. Moreover, while Applicants believe that claims 5 and 6(a-b) were fully enabled as previously worded, "PA" has been replaced with "PA83" (indicated by the Examiner to be enabled), thereby obviating the Examiner's concerns as to those claims. With respect to claims 5-6, Applicants respectfully disagree and traverse as discussed in detail below.

With respect to claim 6(c), Applicants note that Example 5 and Figure 3 of the specification provide enablement for antibodies that inhibit heptamerization of PA63. Example 5 describes the rubidium release assay, in which the intracellular release of radiolabeled ions through the PA63 heptameric pore is measured. Specifically, the specification teaches that upon cleavage of PA into 63kD and 20kD fragments, the PA63 fragment assembles into a heptameric structure that, upon exposure to acidic conditions, forms a transmembranous pore. The presence of pores can then be detected by tracking the amount of an intracellular radiolabel, such as rubidium, released through the pore. *See* paragraphs 366 and 367. Figure 3 shows the results of this assay, in which 25nM of either of two anti-PA monoclonal antibodies, PWD0283 or PWD0587, result in inhibition of rubidium release. Thus, antibodies that inhibit heptamerization of PA63 are enabled.

With respect to claims 6(d-g), the specification also provides experimental evidence that certain antibodies of the invention (PWD0283 and PWD0587) block PA63 binding of EF and LF, as well as PA-mediated translocation of EF and LF across the membrane. Example 7 experimentally demonstrates that the antibodies of the invention bind to the heptamer with high affinity. *See* Table 7. Example 8 and Figure 4 show that the antibodies of the invention are able to block LT mediated cell killing. Specifically, cells that were incubated overnight with either antibody and subsequently exposed to a lethal dose of LF exhibited a high survival rate, indicating that LF did not undergo endocytosis and cytoplasmic release. *See* paragraphs 378 and 379. Example 13 shows that EF is inhibited from translocating across the membrane in the presence of the antibodies of the invention. Specifically, cells incubated with either antibody fail

to develop high levels of intracellular cAMP, a hallmark sign of EF cellular entry. *See* paragraphs 415-419. Taken together, this experimental evidence illustrates that the antibodies of the invention bind to the PA63 heptameric complex, block binding of LF and EF, and inhibit the translocation of EF and LF across the membrane. Therefore, the specification amply enables antibodies that inhibit heptamerization of PA63, PA63 binding to EF or LF and inhibition of PA-mediated translocation of EF or LF across a membrane.

In light of the above, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Conclusion

Entry of the above amendment is respectfully solicited. In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the allowance of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an additional extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Dated: October 28, 2008

Respectfully submitted,

/Mark J. Hyman/
Mark J. Hyman
Registration No.: 46,789
HUMAN GENOME SCIENCES, INC.
14200 Shady Grove Road
Rockville, Maryland 20850
(240) 314-1224

MJH/JE/BA